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ÆTIOLOGY AND PATHOLOGY OF EXTRA-UTERINE PREGNANCY.*

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Ætiology.—The ætiology of extra-uterine pregnancy can not be definitely stated until we have a more exact knowledge of the process of impregnation in normal pregnancy. It will be necessary to consider the latter in a few words. The ovum is normally carried into the uterus by the ciliary movement of the epithelial lining of the tube and by the peristaltic action of the tube toward the uterus. Added to this there may be some mechanical influence exerted by the peristalsis of the intestines, the force of gravity, resp ration, capillary attraction, and voluntary movements of the muscles. This part of the migration of the ovum is much more easily explained than is the manner in which it reaches the tube.

The theory of the erectile nature of the fimbriæ and the ejaculation theory in which the ovum is in the first case drawn into the tube by the retracting arms and in the second hurled out of the follicle with considerable force, have been practically abandoned. The most natural course would seem to be the following: A ripe follicle bursts, and the ovum, surrounded by a somewhat sticky fluid, slowly emerges to the surface of the ovary. From here it may take two different courses: it may either get into the peritoneal cavity and die, or it may be taken along by the capillary stream until it meets one of the fimbriæ, and from there it will be helped into the pavilion of the tube by the ciliated epithelium.

The next consideration of importance is the place of impregnation. Nature has provided in the voluminous folds of the distal end of the tube an excellent meeting place for spermatozoön and ovum, and, if an analogy may be drawn from many experiments on animals,

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this is the place where fertilization usually takes place. The ætiological factors that would favor a lodgment of the fertilized ovum outside of the uterus—that, in other words, would cause an extra-uterine pregnancy—must be looked for either in the ovum itself or in the path along which it must travel to the uterus. Perhaps too little attention has been paid to a possible pathological condition of the ovum as a cause of ectopic pregnancy. The ovum, when discharged from the follicle, is surrounded by a structureless granular layer of protoplasm, which may have some function in permitting an easier coaptation of the ovum to the place where it finally becomes imbedded. How far a pathological condition of the ovum may influence this granular layer to premature activity is at present only a subject for conjecture.

A second ætiological factor may be found in an antiperistaltic movement of the tube. This may occur in consequence of fright or excessive sexual excitement, and may cause an ectopic imbedding of the ovum. The vast majority, however, of ectopic pregnancies point to a pathological condition of the tube as the primary ætiological factor.

Until recently the generally accepted opinion was that the destruction of the mucosa of the tube was necessary for the imbedding of the ovum. This was founded on the assumption that in normal pregnancy the most favorable condition for the lodgment of the ovum was created by the menstrual shedding of a part of the uterine mucosa. Bland Sutton (1), Veit (2), Hofmeier (3), Webster (4), Martin (5), and others have found that the mucosa is nearly normal at the place of insertion of the ovum. In other words, as an ovum will not imbed itself in a uterus whose mucosa is diseased, it will not imbed itself in an entirely diseased tube. The tube may contain evidences of acute or chronic salpingitis in many places, but at the place of imbedment of the ovum it is healthy. It is quite evident, however, how the various forms of salpingitis may form ætiological factors in ectopic lodgment of the ovum. The ciliæ may be destroyed to a greater or less extent and the ovum thus deprived of this necessary propelling force ; or the tube may become partly occluded, permitting the passage of the spermatozoön only ; or, finally, it may be closed completely, and fertilization may take place by the passage of the sperma through the healthy tube and across the abdominal cavity. Hernial pouches of the tube produced by protrusion of the mucous membrane through separated bundles of muscular fibers, as well as accessory tubes, constitute further predisposing conditions to ectopic gestation, and, finally,

mechanical obstructions other than those caused by inflammations within the tube itself may be present. In this category may be mentioned :

1. Abnormal convolutions of the tube due to congenital malformation.

2. Enlargement of the organs surrounding the tube.

3. Old inflammatory bands and adhesions.

Pathological Anatomy.—According to the place of attachment of the ovum, we make the classification of tubal, ovarian, and abdominal pregnancy. The first of these is again subdivided by the natural division of the tube into three classes—interstitial, isthmic, and ampullary pregnancy.

1. Interstitial pregnancy is not very frequent and is often confounded with pregnancy in the horn of a rudimentary uterus. According to Haecker (10), it occurs principally in women who have had several children. The left side is more frequently affected than the right ; in seventeen out of twenty-four cases Haecker found it insolvent. In the beginning of pregnancy a swelling in the horn of the uterus is noticeable, which becomes more sharply marked as pregnancy advances. The round ligament has a characteristic position. It lies lateral to the fœtal sac, whereas in tubal pregnancy it is the median line. In its further development the interstitial pregnancy may approach nearer to the uterus and a tubo-uterine pregnancy may result.

2. Isthmic pregnancy may occur in the portion of the tube between the ampulla and the uterine insertion. This usually takes place in the middle of the tube, which is enlarged and fusiform in shape. The wall of the tube is either universally hypertrophied, or is thinned out at one particular spot. According to Werth, the posterior wall of the tube has a peculiar disposition to become thinned out.

3. Ampullary pregnancy is by far the most common form of ectopic pregnancy. If the ovum is lodged near the infundibulum of the tube, it may partly project into the abdominal cavity and give rise to a tubo-abdominal pregnancy, or it may lodge partly on the ovary and be called tubo-ovarian pregnancy.

So-called secondary forms of tubal pregnancy may occur in the following varieties : (*a*) intraligamentous and (*b*) secondary abdominal. In the first variety the ovum in its development gradually separates the two folds of the broad ligament, and as the muscular elements of the tube thin out they may finally disappear altogether, so that the fœtal sac is formed entirely by broad-ligament folds, or the

ovum may rupture the tubal wall and lodge between the folds of the ligament underneath the tube. Secondary abdominal pregnancy will occur either when the fruit sac ruptures or when the ovum makes its exit entirely or in part through the abdominal end of the tube.

The course which extra-uterine pregnancy takes may be varied. All forms may be carried on to term, or may even remain in the body for years after the death of the fœtus. In the majority of cases, however, the pregnancy is interrupted during the first four months. Either rupture of the sac or absorption of the ovum takes place. To the latter condition especial attention has been called by Werth (7). Without causing rupture of the sac walls, a considerable hæmorrhage may arise from the place of insertion of the ovum after the death of the fœtus, which will usually flow through the abdominal ostium of the tube into the cavity and produce an intraperitoneal hæmatocele, or, if the ostium be closed, will produce a hæmatosalpinx. The causes assigned for the rupture of the tube are the increased pressure on the one hand and the weakening of the tubal walls through the penetrating chorionic villi on the other. When the latter undergo degeneration, as is often the case, this weakening influence is especially pernicious.

The origin of the hæmorrhage is in the placenta, and from there the blood flows in the direction of least resistance. The rupture of the fœtal sac is not always coincident with the rupture of the tube; in fact, the fœtal membranes seem to possess a greater power of resistance than the more friable tissues of the tube.

The tubal abortion may be of two kinds; either complete, in which the ovum is cast out entirely with only a few chorionic villi remaining, or incomplete—that is, more or less of the ovum is left in the tube. In both rupture and abortion a blood clot will be found at the place of insertion of the ovum, which may, especially in abortion, attain great dimensions. In these coagula may be noticed occasionally several concentric layers of different colors, showing that hæmorrhages have occurred at different periods. In every rupture and in most abortions we find that a free hæmorrhage has occurred in the abdominal cavity, which upon coagulation produces either a hæmatocele or a hæmatoma in the broad ligament.

I come now to some characteristic changes in those parts of the genital tract not directly affected by the pregnancy. All the organs participate in the hypertrophy. The vagina widens, its lumen becomes greater, the mucosa is more succulent and takes on a livid discoloration.

The changes in the uterus are more marked and more constant.

It becomes hypertrophied, the musculature thickens, the cavity enlarges, and the cervix becomes soft and patulous. The most conspicuous changes occur in the mucosa of the uterus and the upper portion of the cervix. This partakes entirely of the nature of a decidua, which is expelled at the death of the fœtus or at the end of pregnancy. This decidua is very constant. In forty cases Haecker (10) found only three in which it was not present. In these three the enlarged uterus showed a smooth surface covered with a slightly sanguinolent mucus. If the decidua is present, the mucosa has no smooth surface, but is furrowed by more or less deep grooves.

The microscopical appearances of the mucosa in ectopic pregnancy was first clearly described by Ercolani and afterward by Langhans (11), Leopold (9), and many others. Langhans found in a two months' tubal pregnancy almost the identical condition that the mucosa presents in a four months' intra-uterine pregnancy. Three layers can be plainly discerned. A deeper one, in which the glands are slightly developed; a middle layer, in which they are greatly widened out; and a superficial one, in which there is a very compact layer of large decidual cells. He found the boundaries of these layers less strongly marked than in normal pregnancy. The nearer to the uterus the implantation of the ovum, the more conspicuous are these changes in the mucosa. The musculature likewise hypertrophies.

The uterus may attain a length of from ten to eighteen centimetres. Having attained a certain size, corresponding to about the third month of normal pregnancy, its development stops, and frequently even involution takes place. The latter is always the case as soon as the extra-uterine pregnancy is arrested in its development. In the latter case the uterine decidua is thrown out, generally in its entirety, presenting a perfect cast of the cavity. The decidua is from three to seven millimetres thick.

Microscopic changes in the ovum are as follows: The chorionic villi are covered by a double layer of epithelium, one arising from the fœtus, and the other, the so-called syncytium, from the tube. In the examination of coagula derived from an extra-uterine pregnancy great importance attaches to the finding of chorionic villi. Decidual cells are only rarely found, but that they are found in tubal pregnancy is admitted by all investigators. The origin of the decidua is explained in three different ways:

1. From white blood-corpuscles.
2. From glandular epithelium.
3. From connective-tissue cells.

The consensus of opinion seems to favor the latter way. The connection between the chorion and decidua serotina is not so intimate as in uterine pregnancy. The formation of a decidua vera is confined to the immediate neighborhood of the ovum. The presence of a reflexa can undoubtedly be proved in a great many cases. The further development and construction of the placenta is exactly the same as in uterine gestation.

Microscopic findings in the fruit sac are as follows: In most freshly ruptured cases hyperplasia and hypertrophy of the muscular elements of the tube can be found. With increasing growth of the ovum the fruit-sac walls become continually thinner, so that in some places the wall consists only of fibrillary connective tissue, the muscular elements disappearing completely. The vessels are always found in great abundance, and we often notice hæmorrhages into the surrounding connective tissue. The muscular hypertrophy may, however, continue until the end of pregnancy.

The peritonæum gives rise to many interesting changes. Fibrinous exudates are frequently found on the peritoneal covering of the affected organ, which may cause pseudo-membranes and adhesions with neighboring organs. Occasionally hypertrophy of the peritoneal epithelium has been found, a condition which Walker (6) and Dobbert (12) have described as characteristic of abdominal pregnancy. The enormous vascularity is also much marked.

Although the cases are few, there are undoubtedly some reliable reports of ovarian pregnancy. The ovary forms the fœtal fruit sac and enlarges accordingly. Three distinct layers are described: An outer layer, poor in cells; a middle layer, rich in cells and containing numerous corpora lutea; and lastly a layer of endothelial cells lining the cavity of the fruit sac.

The fruit sac in abdominal pregnancy shows varied formations. Cases have been described in which the ovum was found in a peritoneal sac, shut off entirely from the rest of the cavity. The placenta was inserted in the wall of this sac. In a second variety of cases the ovum was also shut off from the general peritoneal cavity by adhesions of the neighboring intestines, mesentery, and peritonæum. A third variety has been reported in which only a partial shutting off was effected by intestinal adhesions, and finally some cases have been observed in which the chorion, amnion, placenta, and fœtus lay free in the abdominal cavity. The critique of the cases of abdominal pregnancy must be very strict, and all cases in which muscular fibers are said to have been found in the sac wall may be considered to

have had a primary tubal origin. Undoubtedly an analogous condition is found in the lower animals, but this is more easily accounted for by the less firm insertion of the placenta. A perfectly described case of undoubted abdominal pregnancy does not exist.

Fate of the Fœtus.—In all cases of undisturbed ectopic pregnancy the fœtus dies sooner or later, with the exception of the very rare cases of interstitial pregnancy, where the fœtus may develop toward the uterine end of the tube and finally escape *per vias naturales.* Dissection has shown that the deaths have been due to asphyxiation. If the fœtus gets into the abdomen in the early part of its existence, it may be completely absorbed.

In older fœtuses we find either a sort of mummification leading to a formation called lithopædion, or a maceration of the soft parts, only the bones remaining. In the latter condition suppuration and breaking through into neighboring organs may result. The lithopædion formation is certainly a less dangerous condition, and a fœtus thus changed may remain in the body indefinitely.

It must, in conclusion, be mentioned that in most fœtuses carried to term, we find some sort of malformation in consequence of the cramped conditions and the impaired nutrition.

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